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(57) Abstract

Polymeric compositions containing antimicrobial agents and methods for making and using same are provided. The antimicrobial agents include phytochemicals and phytonutrients such as naturally occurring extracts from plants and herbs and other chemical disinfectants safe for use on food–contact surfaces. Chemical releasers can be added to the compositions for causing the release of the antimicrobial agents. The chemical releasers include citric acid extract. A blend of antimicrobial agents can be included in the composition for destroying and inhibiting the growth of a wide variety of different microorganisms including bacteria, viruses, and fungi.

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POLYMERS CONTAINING ANTIMICROBIAL AGENTS AND METHODS FOR MAKING AND USING SAME

Field of the Invention

This invention relates generally to compositions containing biocidal agents and more specifically to polymeric substrates containing phytochemicals exhibiting biocidal activity. In particular, the biocidal agents of the present invention are believed to be safe for human contact, in at least one embodiment, safe for contact with food, and in one preferred embodiment, are derived from natural ingredients or from compositions known to be non-toxic.

Background of the Invention

In recent years, polymers and plastics have become increasingly popular and important materials for making various types of articles. These articles, in turn, have been used in a limitless variety of applications. For instance, polymers and plastics are typically used as containers for various articles, such as food items. In some applications, an item contained in a polymeric or plastic article can be subject to attack and contamination by microorganisms, as well as undesirable macroorganisms. For example, contaminating microorganisms may include bacteria, algae, fungi and yeasts, viruses, and parasites. Macroorganisms may include, but are not limited to, nematodes, crustaceans (barnacles, for example) and insects. As such, a biocidal polymeric or plastic material capable of destroying or inhibiting

foreign microorganisms and macroorganisms would be highly desirable.

Bacterial contamination of food, especially meat products, has become the focus of growing concern among public health professionals. In 1993, over 500 individuals became ill, and five people died, after eating hamburgers purchased from fast food restaurants. The causative organism, *E. Coli* 0157:H7, is most often associated with ground beef.

Recently, the coccidian parasite *Cyclospora* was implicated in an outbreak of gastrointestinal illness among school children, who had ingested contaminated strawberries served for school lunch. Such infection may result in a protracted illness, characterized by frequent, watery stools and other gastrointestinal symptoms; symptoms which may remit and relapse. Although antibiotic therapy is effective to shorten the clinical course associated with *Cyclospora* infection, no treatment regimen has been identified for patients who cannot tolerate sulfa drugs (*MMWR*, 46:451, May 23, 1997).

Contamination of foodstuffs by viruses and parasites has recently become of growing concern, because the resulting infections often are refractory to drug treatment. In the majority of persons, the body's immune system is able to limit the replication of such infectious agents, leading to the eventual control and resolution of clinical disease. However, in immunocompromised individuals, such as those suffering from cancer or AIDS, the immune system may not be able to control infection,

resulting in a much more serious prognosis.

Although some of the problems associated with microbial contamination of food can be addressed by improved handling and preparation techniques, methods which would reduce contamination during packaging and storage would also significantly decrease the risks associated with food-borne contamination.

A number of methods have been proposed to reduce microbial contamination in foodstuffs prior to preparation. Improvements in poultry processing methods, for example, have reduced the risk of salmonella food poisoning. However, contamination still occurs and any microorganisms present will continue to replicate once the meat is packaged. Thus, special care is still required during storage and handling to prevent food poisoning caused by the ingestion of pathogenic microbes.

During packaging, the treatment of foodstuffs with agents capable of reducing or eliminating microorganisms would decrease the risks associated with food-borne illnesses. However, most of these agents are themselves associated with unacceptable safety risks.

For example, irradiating fruit and milk has been shown to reduce microbial contamination, but safety concerns have prevented the wide-spread acceptance of irradiated products.

The use of antimicrobials could also effectively reduce contamination associated with foodstuffs. However, because the use of such drugs

has been associated with the development of resistant organisms, such an approach is currently impractical.

However, many naturally occurring plants and herbs have been shown to possess antimicrobial activity and their use has been shown to be safe for human and animal consumption. Extracts of such plants and herbs, known as phytochemicals or phytonutrients, may be useful to reduce microbial contamination during the processing and storage of foodstuffs, while providing the added advantage of being safe for contact with consumables. Additionally, phytochemicals are known which have broad activity, preventing or inhibiting the growth of not only microbial contamination, but also macrobial infestation by nematodes, insects, larvae and crustaceans.

The present invention is concerned with reducing contamination of organic materials, including but not limited to the processing and storage of foodstuffs. Other uses include treating bio-fouling problems resulting from biofilm production on equipment in a variety of marine, industrial and residential settings; preventing or reducing contamination on medical equipment and devices; and eradicating or impeding insect, nematodal, or crustacean infestation. Current solutions often involve the use of toxic chemicals, creating exposure and disposal concerns. For example, the prevention of bio-fouling often involves applications of toxic chemicals to marine

surfaces, resulting in the accumulation of biohazardous waste material.

Current medical practice aimed at reducing or preventing microbial contamination often involves the use of prophylactic antibiotics, however concerns relating to the increase in resistant organisms due to antibiotic overuse, has made alternative solutions desirable.

In general terms, the present invention relates to the incorporation of biocidal phytochemicals into polymeric materials, such that the activity of the agents will reduce the microbial and macrobial contamination of the organic material with which it comes in contact. In a particular application for plastic food wrappers, phytochemicals with antimicrobial activity are mixed with polymer compositions during formation of the plastic sheeting and molded containers and thereafter reduce or destroy the bacteria on that portion of the foodstuffs with which it comes into contact. Plastic sheeting for food wrappers and plastic containers are only two specific applications for the composition of the present invention.

The prior art discloses a number of examples of plastic materials containing biocidal agents, but none have the particular characteristics of the present invention.

For instance, U.S. Patent No. 5,554,373 to Seabrook et al., which is incorporated herein by reference in its entirety, discloses compositions

containing antimicrobial agents and a chemical controller, which functions to regulate the release rate of the antimicrobial agent. One of the biocidal agents disclosed is 10,10-oxybisphenoxarsine, which is an organically bound arsenic and will be referred to hereinafter as OBPA.

U.S. Patent No. 4,888,175 to Burton, et al., discloses a plastic packaging material having a biocidal agent dissolved or dispersed therein. The biocidal agent disclosed is OBPA. The plastic material can be formed into a package for containing an organic material susceptible to bacterial or viral attack.

U.S. Patent No. 4,666,956 to Spielau, et al. discloses a biocidal composition based on organic arsenic compounds. A tin compound is added to the composition to prevent elution of the arsenic compound. The compositions are used in the production of molded plastic articles, especially those vulnerable to biological attack.

U.S. Patent Nos. 4,624,679 and 4,891,391, both to McEntee, disclose an antimicrobial and anti-oxidant composition preferably incorporated into a thermoplastic resin. The antimicrobial agents are incorporated into the thermoplastic materials during fabrication so that the resulting thermoplastic articles will resist microbial growth. The anti-oxidant is added so that the antimicrobial agent does not degrade during processing. OBPA is disclosed as one of the

microbiocides.

An assortment of compositions containing microbiocides are disclosed in U.S. Patent Nos. 4,686,239, 4,789,692, 4,086,297, and 4,663,077 in which Rei is listed as an inventor. In the '239 patent, the '692 patent, and the '297 patent, a composition is disclosed wherein a microbiocide in high concentrations is added to a thermoplastic resin. The resulting concentrate is then incorporated into a second thermoplastic resin to produce a resulting article having the appropriate level of microbiocide. The second thermoplastic resin is added in an attempt to control the mobility of the microbiocide. One of the microbiocides disclosed is OBPA.

The '077 patent discloses a microbiocidal solution comprising an aryl alkanol solvent and a microbiocide compound dissolved therein. A plasticizer suitable for use as a polymer processing aid is added to the composition.

Anti-bacterial materials and antimicrobial mixtures are disclosed in United Kingdom Patent No. 1,169,288 and European Patent Application No. 84113170.9. The United Kingdom patent is directed to a material having a base sheet of plastic coated on one surface with a polymeric liquid composition containing an anti-bacterial agent capable of migrating through the sheet. The European patent application, on the other hand, discloses a mixture of a phenoxyarsine as an antimicrobial agent and a solvent. A plasticizer can be added to the mixture

for incorporation into plastics.

Other prior art compositions containing biocides include U.S. Patent No. 4,747,902 to Saitoh, U.S. Patent No. 3,864,468 to Hyman et al., U.S. Patent 4,666,706 to Farquharson et al., U.S. Patent No. 5,063,706 to Aki et al., and U.S. Patent No. 4,876,070 to Tsukahara et al.

Although the prior art shows a combination of biocidal compositions, the particular features of the present invention remain absent. Some of the prior art discloses materials containing small amounts of biocidal compositions for preventing bacterial attack on the material itself. However, most of the prior art does not show the use of biocidal materials in packaging films or sheets at a level such that the contents of the package, instead of the plastic itself, are inhibited against bacterial or viral growth. Further, the prior art is generally deficient in affording a composition that will not only control bacterial growth, but will also simultaneously control the growth of fungi, viruses, and parasites.

Although it is known in the prior art to incorporate biocidal agents into plastics, the plastic products generally cannot be used for food applications unless extremely small amounts of biocides are used because the biocides may be harmful to humans. However, small quantities of biocide will not protect the contents of the package adequately or protect the contents for an effective length of time from attack.

Consequently, a need exists for a polymeric material containing biocidal agents which is safe for human and animal contact and which is safe for contact with human and animal consumables. Further still, although some of the prior art discloses the incorporation of biocidal agents with activity specifically against bacteria, a need exists for a biocidal composition that will simultaneously inhibit the growth of fungi, viruses, actinomycetes and parasites, as well as bacteria.

Summary of the Invention

The present invention recognizes and addresses the foregoing disadvantages, and others of prior art constructions and methods.

Accordingly, one object of the present invention is to provide a biocidal composition.

Another object of the present invention is to provide a biocidal composition containing phytochemicals or phytonutrients which may include essential oils.

A further object of the present invention is to provide a polymeric composition containing biocidal agents.

Yet another object of the present invention is to provide a polymeric composition containing biocidal agents that will destroy or inhibit the growth of bacteria, viruses, parasites, yeast and fungi, algae, insects, nematodes, mollusks and crustaceans.

Still another object of the present invention is to provide a method for the release of the

biocidal ingredient from the phytochemical agent in a polymeric composition.

The present invention achieves the foregoing and other objectives by providing a biocidal agent which, when added to polymeric materials, destroys or inhibits the growth of microorganisms and macroorganisms. Of particular advantage, the biocide included in the invention may be a naturally occurring phytonutrient or phytochemical or it may be a chemical compound shown to be safe for contact with human consumables. As used herein, a phytochemical refers to a naturally occurring chemical or compound derived or extracted from an organism, such as a plant.

In one embodiment, the biocidal agent of the present invention may be added to a polymeric substrate in combination with a migration control agent which controls the rate at which the biocide is released from the plastic or, alternatively, with a chemical releaser which facilitates release of the biocide. Vitamin E may be added to the polymer substrate in order to control the migration and release of the biocidal agent, such as is claimed in the present inventor's previous patent (U.S. Patent No. 5,554,373) as referenced above. Vitamin E is a well-recognized antioxidant, and may function as a release agent by preventing oxidation damage to the biocidal agent.

In another embodiment, the biocide may be the same as the release agent. In addition to functioning as a release agent, Vitamin E possesses

antimicrobial properties, and thus may itself function additionally as the biocide. The following lists other phytochemicals which are known to possess antimicrobial activity as well as function as anti-oxidants (*denotes significant activity): *Panax ginseng; Panax quinquefolius; Bixa orellana; Humulus lupulus; Spinacia oleracea; Arctium lappa; Cichorium intybus; Cynara scolymus; Helianthus annuus; Inula helenium; Armoracia rusticana; Momordica charantia; Vaccinium corymbosum; Vaccinium myrtillus; Avena sativa; Oryza sativa; Lavandula latifolia; Marrubium vulgare; Melissa officinalis; Mentha pulegium; Mentha spicata; Nepeta cataria; Ocimum basilicum; Origanum onites; Perilla frutescens; Prunella vulgaris; Rosmarinus officinalis; Salvia officinalis; Salvia sclarea; Satureja hortensis; Thymus vulgaris; Laurus nobilis; Arachis hypogaea; Glycine max; Glycyrrhiza glabra; Glycyrrhiza uralensis; Lens culinaris; Phaseolus coccineus; Phaseolus lunatus; Phaseolus vulgaris; Phaseolus vulgaris;* Pisum sativum; Psophocarpus tetragonolobus; Pueraria lobata; Tamarindus indica; Tamarindus indica;* Vicia faba; Vigna angularis; Vigna mungo; Vigna radiata; Allium ampeloprasum; Allium cepa; Allium sativum; Asparagus officinalis; Linum usitatissimum; Morus alba; Eucalyptus globulus; Pimenta dioica; Syzygium aromaticum; Olea europaea; Oenothera biennis; Sesamum indicum; Plantago asiatica; Fagopyrum esculentum; Prunus cerasus; Prunus spinosa; Rosa canina; Rubus fruticosus; Rubus idaeus; Coffea*

arabica; Citrus aurantium; Citrus paradisi; Ribes nigrum; Ribes rubrum; Capsicum frutescens; Solanum tuberosum; Solanum tuberosum; Theobroma cacao; Camellia sinensis; Coriandrum sativum; Cuminum cyminum; Daucus carota; Trachyspermum ammi; Vitis vinifera; Curcuma longa; Zingiber officinale.*

Alternatively, or in addition to using Vitamin E, citric acid may also be added to the polymer substrate. Citric acid, which is also an effective antimicrobial agent, has been found to facilitate the release of some biocidal agents.

For many applications, the biocides of the present invention are incorporated into a polymeric composition such that the active concentration of the biocide is at a level capable of inhibiting the growth of micro- or macroorganisms, but is also at a level safe for human handling and consumption and for contact with consumables.

As used hereinafter, the term active concentration refers to the concentration of the biocidal agents that are available for destroying and inhibiting the growth of microorganisms and/or macroorganisms. The active concentration further refers to the biocidal agents that have been released from the materials in which they are contained. Also, the term consumables as used hereinafter is defined as any food product, including, but not limited to, agricultural products. Consumables also refers to all drinkable liquids, including water.

The present invention is directed to a biocide

for adding to polymeric materials for protecting such materials and other items in close proximity thereto from attack and infestation of micro- and macroorganisms. In one embodiment, the biocide of the present invention may include capsaicinoids, which are phytochemicals derived from the fruit of Capsicum frutescens. Capsaicinoids can inhibit or destroy bacteria, viruses, fungi, crustaceans, and mollusks, among other organisms. Available commercially as oleoresin capsicum, capsicum can be added to a polymer in a liquid carrier or can be incorporated via dry soluble carriers such as salt or dextrose. Preferably, a 4% (weight/volume) solution of capsicum is added to an equal volume of a vegetable oil, such as soybean oil and particularly epoxidized soybean oil, with the resulting mixture being added to the polymer during extrusion. The capsicum can be added as a 4% solution to polymeric materials in an amount from about .05 ppm to about 10 ppm, for food applications; from about 10 ppm to about 100,000 ppm, for industrial and marine applications; and as solutions of 2%, 4%, 12% or 14%, from .05 ppm to about 50,000 ppm, for medical and agricultural applications.

In an alternative embodiment, the biocide may include grapefruit seed extract, which exhibits anti-bacterial, anti-parasitic, and anti-fungal activity. The grapefruit seed extract, available commercially as CITRICIDAL, can be added in a liquid carrier. The liquid carrier can be

propylene glycol, polyethylene glycol, or silicone. For example, the grapefruit seed extract can be mixed with propylene glycol, preferably in a 1:1 ratio, before being added to polymeric materials. The grapefruit seed extract can be added to polymeric materials alone, in combination with other biocides, in combination with citric acid, and in combination with Vitamin E. The grapefruit seed extract can be added to polymeric materials in an amount from about 5,000 ppm to about 30,000 ppm for food applications; from about 20,000 ppm to about 50,000 ppm for industrial applications; from 5,000 ppm to about 30,000 ppm for medical applications, and from about 5,000 ppm to about 50,000 ppm for agricultural applications.

In yet another alternative embodiment, the biocide may be a phytochemical-derived formula, commercially known as BIOCIDIN, which exhibits anti-fungal, anti-bacterial and anti-parasitic activity. The BIOCIDIN formula contains: chlorophyll, impatiens, pallida, hydrastis canadensis, ferula galbanum, hypericum perforatum, villa rubris, fumaria, frasera carolinesis, gentiana campestris, sanguinaria, allicin and garlic. BIOCIDIN can be added alone or in combination with other biocides, with Vitamin E, or with chemical releasers, such as citric acid. Further, BIOCIDIN may be added to a polymer carrier, such as an Epoxidized Soybean Oil (ESO) or an Epoxidized Vegetable Oil (EVO). BIOCIDIN may be added to polymeric materials in an amount from

about 2,000 ppm to about 25,000 ppm for food applications; from about 2,000 ppm to about 25,000 ppm for medical applications; from about 5,000 ppm to about 50,000 ppm for industrial applications; and from about 5,000 ppm to about 50,000 ppm for agricultural applications.

In yet another embodiment, the biocide may be Lemon Grass Oil which is another phytochemical. Lemon Grass Oil is a natural by-product of lemon grass and is extracted by steam and other nontoxic extraction methods. Lemon Grass Oil exhibits anti-fungal and anti-bacterial activity. The Lemon Grass Oil may be added to polymeric substrates alone or in combination with other biocides, migration controllers such as Vitamin E, or releasers, such as citric acid, or may be added to a polymer carrier such as ESO or EVO. The Lemon Grass Oil may be added to the polymeric materials in an amount from about 2,000 ppm to 20,000 ppm for food applications; from about 5,000 ppm to about 50,000 ppm for industrial applications; from about 2,000 ppm to about 50,000 ppm for medical applications and from about 2,000 ppm to about 50,000 ppm for agricultural applications.

In another alternative embodiment, the biocide may be Tea Tree Oil, which is also a phytochemical. Tea Tree Oil is a natural by-product of the tea tree, (*melaleuca* species). Tea Tree Oil is extracted through natural non-toxic precesses such as steam. Tea Tree Oil exhibits anti-fungal and anti-bacterial activity. Tea Tree Oil may be added

to polymeric substrates alone or in combination with other biocides, migration controllers such as Vitamin E or releasers such as citric acid, and may be added to a polymer carrier, such as ESO or EVO. Tea Tree Oil may be added to the polymeric materials in an amount from about 2,000 ppm to about 20,000 ppm for food applications; from about 5,000 ppm to about 50,000 ppm for industrial applications; from about 2,000 ppm to about 50,000 ppm for medical applications and from about 2,000 ppm to about 50,000 ppm for agricultural applications.

In yet another alternative embodiment, the biocide may be a chemical biocide, which has been shown to be safe when used in contact with food. For instance, the chemical biocide may be trichloromelamine (N-chloro-p-toluenesulfonamide sodium salt-trihydrate), which exhibits bacteriocidal activity against both gram positive and gram negative bacteria. Trichloromelamine can be added as a powder or in a liquid carrier, such as epoxidized soybean oil, vegetable oil or propylene glycol. Trichloromelamine can be added as a 60% (weight/volume) concentration to polymeric materials. The trichloromelamine may be added alone or in combination with other agents, including phytochemical biocides and with or without citric acid to facilitate the release of the active biocidal agent in trichloromelamine or to control a broader range of microbes. Trichloromelamine can be added to polymeric materials in an amount from

about 50 ppm to about 50,000 ppm, preferably in an amount from about 50 ppm to about 5000 ppm for food applications; and from about 10,000 ppm to about 50,000 ppm for industrial, medical, or agricultural applications.

In another alternative embodiment, the biocide may be zinc pyrithione, which exhibits anti-bacterial activity. The zinc pyrithione may be added to polymeric materials alone or in combination with other biocides, and with or without Vitamin E. The zinc pyrithione can be added to polymeric materials in an amount from about 5,000 ppm to about 30,000 ppm for food applications; from about 20,000 ppm to about 50,000 ppm for industrial applications; from about 5,000 ppm to about 30,000 ppm for medical applications; and from about 5,000 ppm to about 50,000 ppm for agricultural applications.

Another group of chemical biocides that may be used according to the present invention and which have been shown to be relatively safe are the quaternary ammonium compounds. For instance, particular examples of quaternary ammonium compounds that may be incorporated into polymers for providing the polymers with antimicrobial properties are alkyl dimethyl benzyl ammonium chloride (ADBAC), dialkyl dimethyl ammonium and alkyl dimethyl ethybenzyl ammonium chlorides.

As described above, the present invention includes a chemical releaser, which is used to facilitate the release of the antimicrobial agents

from the polymeric material. In particular, in some applications, the chemical releaser allows the active ingredient contained in the biocide to be released from the polymeric substrate. The releaser may be citric acid, a phytochemical which also exhibits anti-bacterial activity. For example, citric acid can facilitate the release of chlorine from tricloromelamine embedded in polymeric materials, resulting in an increase in the active concentration of the biocidal agent. Citric acid extract can be added in a liquid carrier. The liquid carrier can be propylene glycol. Citric acid extract can be added to polymeric materials alone or in combination with other biocides. Citric acid extract can be added to polymeric materials in an amount from about 5,000 ppm to about 30,000 ppm for food applications; from about 20,000 ppm to about 50,000 ppm for industrial applications; from 5,000 ppm to about 20,000 ppm for medical applications, and from about 5,000 ppm to about 50,000 ppm for agricultural applications.

In an alternative embodiment, starch may be added as a chemical releaser, functioning to release the biocidal agent as the starch polymer degrades.

It should be understood that the present invention is generally directed to the use of biocides in polymeric substrates such as phytochemical biocides and other antimicrobial agents that have been proven to be safe when used

in contact with food items. The various biocides and antimicrobial agents mentioned above represent various preferred embodiments of the present invention. The amounts and concentrations listed above are also merely exemplarily and may be increased or decreased depending upon the particular application. Other biocides that may be used in the process of the present invention will be discussed in greater detail below.

The polymeric material that can be combined with the biocides of the present invention include, for instance, silicone products, such as N-propylsilicate, a polyalkylene, a polyolefin, a polyvinyl, a synthetic rubber, a latex fiber, epoxies, or mixtures thereof.

The polymeric material, which serves as a substrate for the addition of the biocidal agent, can be blown, extruded, molded or otherwise manufactured into a variety of applications, including sheets, molded articles, fibers, coatings, sprays, adhesives, epoxies, laminates, glues, gels, and acrylics.

In alternative embodiments, the biocide can be a phytochemical incorporated into thermoset and thermoplastics, used in molded devices (both reinforced and non-reinforced), used to coat natural fibers or incorporated into synthetic or processed fibers, or incorporated into polymeric coatings, sprays, adhesives, gels, or acrylics.

Once a biocide has been incorporated into a polymeric material in accordance with the present

invention, the polymeric material can be formed into various articles for a limitless variety of applications. For instance, the article can include plastic sheeting wherein the biocidal agents can prevent the growth of bacteria, viruses, algae, fungi, and other organisms on the sheeting or in contact with the sheeting. Such a sheeting can be used for a variety of applications, including food wrap; greenhouse plastic; liners for plant pots, swimming pools and hot tubs; and counter-surface liners.

In an alternative embodiment, the polymeric article can be manufactured in the form of agricultural granules for protecting agricultural products from attack by micro- or macroorganisms, or can be molded in the shape of a plant container, plant starter pot, or plant tray for protecting a plant from infection and infestation.

In yet another embodiment, the polymeric article containing the biocide can be formulated in a variety of ways for medical and industrial applications. For example, the phytochemical can be incorporated into the polymer and administered as a spray, an adhesive, a laminate or a coating, to prevent or reduce contamination in marine, industrial and medical settings. Water treatment facilities and pipes can be treated with a polymeric spray containing a biocide, with or without a release agent, to prevent or reduce contamination from algae, crustaceans, and/or bacteria.

The present invention is further directed to a method of controlling the release of biocidal agents from a polymeric composition. The method includes the steps of providing a polymeric material capable of being formed selectively into granules, films, sheets, tubing and other various articles. Biocidal agents, such as capsicum, grapefruit seed extract, citric acid, BIOCIDIN, Lemon Grass Oil, Tea Tree Oil, Vitamin E, zinc pyrithione, quaternary ammonium compounds and trichloromelamine, can be incorporated into the polymeric material. In particular, the biocidal agents are incorporated into the polymeric material in an amount so as to prevent or inhibit the growth of micro- or macroorganisms on, or in close proximity to, the polymeric material.

Other objects, features, and aspects of the present invention are discussed in greater detail below.

Brief Description of the Drawings

A full and enabling disclosure of the present invention including the best mode thereof to one of ordinary skill in the art, is set forth more particularly in the remainder of the specification, including reference to the accompanying figures in which:

Figure 1 is a plan view of a sheet prepared in accordance with the present invention.

Figure 2 is a perspective view of a roll of polymeric film made in accordance with the present invention.

Figure 3 is a perspective view of a box liner made in accordance with the present invention.

Figure 4 is a perspective view of a pot for a plant in accordance with the present invention.

Figure 5 is a tray for plants for germination of seeds made in accordance with the present invention.

Repeat use of reference characters in the present specification and drawings is intended to represent same or analogous features or elements of the invention.

Detailed Description of Preferred Embodiments

In general terms, the present invention is directed to polymeric compositions containing biocidal agents and methods of making and using the same. The rate of migration or the release of the biocidal ingredient embedded in the polymeric composition may be affected by using a release agent, such as a migration controller such as Vitamin E, a chemical releaser such as citric acid, or an anti-oxidant such as Vitamin E. In an alternative embodiment, the chemical releaser may be the same as the biocidal agent. One of the important advantages of the present invention is that the composition can be made into plastic articles to protect food products, medical devices, plants and other agricultural products, or act as water lines. In one embodiment, the antimicrobial agents are extracted from naturally occurring substances, such as phytochemicals. These agents may be safer to use in direct contact with

foodstuffs than conventional antimicrobial drugs. Besides phytochemicals, however, the present invention is also directed to the use of various other biocidal agents.

The composition of the present invention is directed to a base polymeric material containing a single or a mixture of biocidal agents. Preferably, these biocidal agents are dispersed within the polymeric base composition. However, the biocides may be applied directly to the polymeric substrate, as with natural fibers impregnated with the biocidal agent. Particular examples of biocidal agents include phytochemicals such as capsaicinoids, grapefruit seed extract, BIOCIDIN, Lemon Grass Oil, Tea Tree Oil, citric acid, Vitamin E and various other antimicrobial agents that are believed to be safe for human handling and contact, such as trichloromelamine, quaternary ammonium compounds and/or zinc pyrithione.

Citric acid extract is obtained from a variety of sources, any particular form of which can be used in the present invention. Citric acid extract may facilitate the release of the biocidal ingredient from an antimicrobial composition. One particular class of compounds whose release is facilitated by citric acid extract according to the present invention is trichloromelamine (N-chloro-p-toluenesulfonamide sodium salt-trihydrate). Trichloromelamine is the active ingredient in a variety of disinfectant formulations, and is approved by the Environmental Protection Agency

(EPA) for use on food-contact surfaces. One commercial source for trichloromelamine is from H & S Chemical Company (Cincinnati, Ohio; EPA Reg. No. 65169-1).

Trichloromelamine does not migrate well from polymers when extruded into the polymer. However, the addition of citric acid to the polymeric composition causes the release of trichloromelamine from the polymer matrix.

Another type of biocidal agent according to the present invention is grapefruit seed extract, an effective antimicrobial agent for inhibiting the growth of a plurality of micro- and macroorganisms. Particularly, grapefruit seed extract is an effective phytochemical biocide against bacteria, fungi, and some parasites. Grapefruit seed extract is available commercially as CITRICIDAL, from Bio/Chem Research (Lakeport, CA).

Another class of compounds found to be effective phytochemical biocidal agents are the major capsaicinoids. Capsaicinoids are known to inhibit or destroy bacteria, viruses, and fungi. One particular source of capsaicinoids is oleoresin capsicum, available commercially from Kalsec (Kalamazoo, MI).

In a preferred composition of the present invention, oleoresin capsicum is extruded into the polymeric material. The resulting composition will destroy or inhibit the growth of bacteria, viruses, and fungi. This is particularly important because, in many applications, the object that is to be

protected from microbial infestation is subject to attack from more than one variety and species of microorganisms.

In alternative embodiments of the present invention, other biocidal agents such as BIOCIDIN, Lemon Grass Oil, Tea Tree Oil, zinc pyrithione and quaternary ammonium compounds such as alkyl dimethyl benzyl ammonium chloride, dialkyl dimethyl ammonium, and alkyl dimethyl ethybenzyl ammonium chlorides may be added to polymeric materials as biocidal agents. The following table is illustrative of some of the phytochemicals of the present invention, which exhibit activity against multiple organisms. Each phytochemical is classified as to general activity (anti-bacterial; anti-viral; anti-fungal; anti-crustacean; larvicidal; insecticidal; molluscicidal; or anti-nematodal) and specific examples of organisms against which the phytochemical is active are provided. However, it is to be recognized by one of ordinary skill in the art that the phytochemicals included in the table are provided for illustrative purposes only and are not meant to serve as an all-inclusive listing:

CLASSIFICATION	PHYTOCHEMICAL	KNOWN ACTIVITY
Anti-bacterial	Annona muricata (Annonaceae)	B. subtilis; E. coli
	A.squamosa	B. subtilis
	Panax ginseng (Araliaceae)	E. coli; P. aeruginosa; S.enteritidis
	Capparis spinosa (Capparidaceae)	E. coli
	Calendula officinalis (Compositae)	B. subtilis; S. lutea; S. aureus
	Cynara scolymus (Compositae)	E. coli
	Cucurbita pepo (Cucurbitaceae)	S. aureus ***
	Cymbopogon citratus (Gramineae)	B. subtilis; B. mycoides; S. aureus; E. coli
	Mentha spicata (Labiatae)	E. coli
	Ocimum basilicum (Labiatae)	B. anthracis; B. cereus; S. aureus; B. subtilis; P. aeruginosa; S. pneumoniae; Actinomycetes
	Rosmarinus officinalis (Labiatae)	B. subtilis; B. cereus; P. aeruginosa; S. typhi; S. aureus
	Glycyrrhiza glabra (Leguminosae)	B. subtilis; S. aureus; S. mutans
	Allium sativum (Liliaceae)	B. subtilis;*** H-17(rec+); C. perfringens; E. amylovora; E. coli; K. pneumoniae; X. campestris;
		P. aeruginosa; S. enteritidis; S. aureus; S. sanguis; E. carotovora
	Aloe vera (Liliaceae)	B. subtilis; C. xerosis; P. vulgaris
	Citrus reticulata (Rutaceae)	E. coli; P. vulgaris; P. aeruginosa; S. mutans
	Oenothera biennis (Onagraceae)	S. mutans
	Plantago major (Plantaginaceae)	S. dysenteriae
	Punica granatum (Punicaceae)	B. anthracis; B. subtilis; E. coli; *** K. pneumoniae; P. aeruginosa; S. aureus
	Ribes nigrum (Saxifragaceae)	E. coli
	Camellia sinensis (Theaceae)	Actinomycete sp.; B. pertussis; E. coli; P. shigelloides; P. aeruginosa; S. aureus; V. cholera
	Curcuma longa (Zingiberaceae)	B. subtilis; L. acidophilus; H-17(rec+)
	Zingiber officinale (Zingiberaceae)	B. subtilis; B. anthracis; E. coli; L. acidophilus; S. aureus

CLASSIFICATION	PHYTOCHEMICAL	KNOWN ACTIVITY
Anti-fungal	Annona muricata (Annonaceae)	Penicillium oxalicum
	Panax ginseng (Araliaceae)	Rhizopus nigricans; Saccharomyces uvarum
	Capparis spinosa (Capparidaceae)	Candida pseudotropicalis
	Calendula officinalis (Compositae)	Neurospora crassa; Candida albicans; C. monosa
	Cucurbita pepo (Cucurbitaceae)	Neurospora crassa
	Cymbopogon citratus (Granimeae)	Absidia spinosa; Alternaria solani; Aspergillus niger; Curvularia lunata; Epidermophyton floccosum; Microsporum audouini; Trichophyton mentagrophytes; Candida albicans; Cryptococcus neoformans; Saccharomyces cerevisiae
	Mentha spicata (Labiatae)	A. niger; F. oxysporum; F. sp. Lentis; *** Trichophyton rubrum
	Ocimum basilicum (Labiatae)	Absidia ramosa;*** Alternaria longipes; Aspergillus aegypliacus; A. awamori; Microsporum gypseum; Trichoconiella padwickii; C. albicans; Kloeckera apiculata
	Rosmarinus officinalis (Labiatae)	F. oxysporum; M. icrosporum canis; P. cyclopium; C. albicans; Rhodotorula rubra; T. rubrum
	Glycyrrhiza glabra (Leguminoseae)	Aspergillus auricomus; T. mentagrophytes; C. albicans
	Allium sativum (Liliaceae)	A. aegypliacus;*** A. fumigatus; A. niger; Botryotrichum keratinophilum; E. floccosum; F. moniliforme; F. oxysporum; Geotrichum candidum; M. canis; Nannizzia fulva; Penicillium digitatum; T. rubrum; T. semii; C. albicans; C. krusei; C. pseudotropicalis; C. neoformans; Debaryomyces hansenii; Kloeckera apiculata; Rhizopus rhizopodiformis; T. padwickii
	Aloe vera (Liliaceae)	T. Mentagrophytes
	Sesamum indicum (Pedaliaceae)	Cladosporium cucumerinum
	Punica granatum (Punicaceae)	A. niger; C. albicans***
	Citrus aurantium (Rutaceae)	A. aegypliacus;*** T. rubrum; C. albicans; C. lipolytica
	Citrus reticulata (Rutaceae)	A. niger; P. cyclopium; C. albicans
	Ribes nigrum (Saxifragaceae)	P. digitatum
	Camellia sinensis (Theaceae)	E. floccosum; T. mentagrophytes; S. cerevisiae; Alternaria tenuis
	Curcuma longa (Zingiberaceae)	Debaryomyces hansenii; A. flavus; A. niger; E. floccosum; Trichoderma viride
	Zingiber officinale (Zingiberaceae)	A.niger; A. auricomus; A. flavus; Botrytis cinerea; N. crassa; T. padwickii; C. albicans; S. pastorianus

CLASSIFICATION	PHYTOCHEMICAL	KNOWN ACTIVITY
anti-viral	Annona squamosa (Annonaceae)	HIV-1
	Panax ginseng (Araliaceae)	Adenovirus 3; herpes simplex 1 virus; semlicki-forest virus; rauscher murine leukemia virus
	Capparis spinosa (Capparidaceae)	Hepatitis virus
	Calendula officinalis (Compositae)	Encephalitis virus-unspec.; herpes simplex virus; HIV-1
	Mentha spicata (Labiatae)	Herpes virus type 2
	Rosmarinus officinalis (Labiatae)	Herpes virus type 2
	Glycyrrhiza glabra (Leguminoseae	Rauscher murine leukemia virus
	Allium sativum (Liliaceae)	Cytomegalovirus; herpes simplex 1 virus; herpes simplex 2 virus
	Aloe vera (Liliaceae)	Cytomegalovirus; herpes simplex 1 virus
	Punica granatum (Punicaceae)	Coxsackie B5 virus; hepatitis B virus; herpes simplex 1 virus;*** herpes simplex 2 virus
	Ribes nigrum (Saxifragaceae)	Encephalitis virus (tick-borne)
	Camellia sinensis (Theaceae)	Coxsackie A9 virus; influenza virus A; influenza virus A2 (manheim 57); poliovirus I
	Curcuma longa (Zingiberaceae)	Hepatitis B virus; vesicular stomatitis virus
	Zingiber officinale (Zingiberaceae)	Herpes simplex 1 virus; rhinovirus type 1-B; virus-lpp1; rauscher murine leukemia virus
anti-crustacean	Annona muricata (Annonaceae)	Artemia salina larvae; Artemia salina***
	Zingiber officinale (Zingiberaceae)	Artemia salina
insecticide	Annona muricata (Annonaceae)	Macrosiphoniella sanborni***
	Annona reticulata (Annonaceae)	Macrosiphoniella sanborni;*** Oryzaephilus surinamensis; Tribolium castaneum
	Annona squamosa (Annonaceae)	Callosobruchus chinensis; Drosophila melanogaster; M.Sanborni;*** Musca Domestica; Pediculus Capitis
	Cucurbita pepo (Cucurbitaceae)	Culex quinquefasciatus
	Mammea americana (Guttiferae)	Aedes aegypti;*** Serotoma ruficornis,adults***
	Mentha spicata (Labiatae)	Drosophila auraria; Mites (Pyroglyphidae)
	Ocimum basilicum (Labiateae)	Culex quinquefasciatus
	Rosmarinus officinalis (Labiatae)	Drosophila auraria
	Citrus reticulata (Rutaceae)	Sitophilus granarius
	Curcuma longa (Zingiberaceae)	Macrosiphum euphorbiae

CLASSIFICATION	PHYTOCHEMICAL	KNOWN ACTIVITY
Larvicidal	Annona squamosa	Anopheles stephensi larvae
	Mammea americana (Guttiferae)	Diaphania hyalinata; Laphygma frugiperda***
	Ocimum Basilicum (Labiateae)	Culex fatigans;*** Diacrisia obliqua
	Allium sativum (Liliaceae)	Culex pipiens-quinquefascialus (1st instar larvae)
	Curcuma longa (Zingiberaceae)	Spodoptera litura Larvae
Molluscicidal	Annona squamosa (Annonaceae)	Biomphalaria straminea
	Ocimum Basilicum (Labiateae)	Biomphalaria pfeifferi
	Camellia sinensis (Theaceae)	Biomphalaria glabrata
Antinematodal	Glycyrrhiza glabra (Leguminoseae	Meloidogyne incognita***
	Phaseolus vulgaris (Leguminosae)	Heterodera glycines

***Denotes strong activity for phytochemical

The present invention, however, encompasses the use of many other biocidal agents. Other phytochemicals that can be incorporated as biocides, is not meant to be an all-inclusive list: *Jasonia candicans* (sesquiterpenes, lactones); *Polygonum flaccidum* (flavone and alpha santalene derivatives); *Acalypha wikesiana* (extracts); *Pavetta owariensis* (procyanidins); *Plectranthus hereroensis* (diterpenoids, diterpenes); Moss (Dicranin extract); *Cannabis sativa* (extract); *Gloiosiphonia* spp. (gloiosiphones); *Laminaceae* spp. (extract); *Securidaca* spp.(extract); *Veronia* spp. (extract); *Hyptis umbrose* (umbrosone); *Asclepias syriaca* (milkweed extract); *Tagetes tenuifolia* (thiophene); *Calophyllum inophylloide* (flavonoids); *Tanacetum densum* (sesquiterpene lactones, triterpenoids); *Neorautanenia mitis* (extract); *Premna schimper* (diterpene); *Premna oligotricha* (sesquiterpenes); *Premna oligotricha* (diterpenes); *Jasonia candicans* (essential oils); *Visnea mocanera* (beta-sitosterol, triterpenic betulinic acid, ursolic acid, plantanic acid); *Asteraceae* spp. (terthiophenes and polyynes); *Petalostemum purpureum* (extract); *Camelia sinensis* (catechin); *Helichrysum picardii* (flavonoids); *Helichrysum italicum* (flavonoids); *Corydalis pallida* (protoberberine alkloids); *Shiraia bambusicola* (perylenequinones); *Fraxinum omus* (hydroxycoumarins); *Podocarpus nagi* (totarol and nortiterpene dilactones); *Heterotheca inuloides* (sesquiterpenoids); *Pelargonium*

spp. (essential oils); *Piper sarmentosum* (phenylpropanoids); *Allium* spp. (extract); *Juniperus procera* (diterpenes); *Achillea conferta* (flavonoids, flavones, sesquiterpenoid lactones); *Magnolia virginiana* (lignans, neolignans); *Eucalyptus euglobal* (euglobal); *Armillaria mellea* (armillaric acid); *Dracena mannii* (spirostanol saponin); *Piper aduncum* (chromenes, prenylated benzoic acid); *Rhamnaceae* spp. (cyclopeptide alkaloids); *Buddleja globosa* (verbascoside); *Cephalocereus senilis* (phytoalexin aurone); *Salvia albocaerulea* (diterpene); *Gomphrena martiana* and *Gomphrena boliviana* (extracts); *Paepalanthus* spp. (vioxanthin); *Helichrysum stoechas* and *Helichrysum crispum* (extracts); *Achillea ptarmica* (trans-pinocarveyl hydroperoxides); *Dehaasia incrassata* (alkaloids); *Asteraceae* spp. (extracts); *Arctotis auriculate* (extracts); *Eriocephalus africanus* (extracts): *Felicia erigeroides* (extracts); *Hemerocallis fulva* (phytosterols, fatty acid esters); *Psoralea juncea* (plicatin B); *Pluchea symphytifolia* (caffeic acid esters); *Tovomitopsis psychotrifolia* (Vitamin E derivative); *Celosia argentea* (triterpenoid saponins and flavonoids); *Azadirachta indica* (tetranortriterpenoid, mahmoodin, protolimonoids, naheedin); *Moraceae* spp. (coumarins); *Hypericum erectum* (phloroglucinol derivatives); *Podospora appendiculate* (Appenolides A, B, & C, furanones); *Artemisia princeps* var. *orientalis*, *Artemisia capillaris*, *Artemisia mexicana* and *Artemisia scoparia*

(extract); Paddy malt (mash extract); *Kigelia pinnata* (extract); *Acalypha wilkesiana* (extract); seaweeds, seagrass and lemongrass (essential oils); *Borrieria latifolia, Borreria setidens, Hedyotis diffusa), Hedyotis nudicaulis, Morinda elliptica, Morinda umbellata, Sida rhombifolia,* and *Vitex ovata* (extracts); *Tabebuia impetiginosa, Achyrocline* spp., *Larrea divaricata, Rosa borboniana, Punica granatum, Psidium guineense, Lithrea ternifolia* (extracts); *Lepechinia caulescens, Lepidium virginicum* and *Tanacetum parthenium* (extracts); *Talaromyces flavus* (extracts); *Daucus carota* (extract); *Flabellia petiolata, Caulerpa prolifera, Halimeda tuna, Corallina elongata, Lithophyllum lichenoides, Phyllophora crispa, Cystoseira* spp., *Halopteris* spp., *Codium* spp., *Valonia utricularis, Posidonia oceanica, Zostera noltii* and *Cymodocea nodosa* (extracts); *Centauraea orientalis, Diospyros khaki, Sida hermaphrodita, Forsythia intermedia, Scutellaria polydon, Eugenia malaccensis* and *Eugenia jambolana* (extracts); *Fritillaria L.* spp. (ebeinone, steroidal alkaloids); *Kigelia pinnata, Peperomia pellucida, Populus nigra, Populus balsamifera* and *Populus deltoides* (extracts); *Melaleuca alternifolia* (essential oil); *Elfvingia applanata* (naringenin); *Ficus sycomorus,* grapefruit seed, Garlic, *Allicin,* Peat, *Strophanthus hispidus, Secamone afzeli, Mitracarpus scaberi, Entada abyssinjca, Terminalia spinosa, Harrisonia abyssinica, Ximinea caffra,*

Azadirachta indica, *Spilanthes mauritiana*, *Terminalia spinosa* (extracts); Cyanobacteria (ambigols A and B, tjipanazole); coffee (extract); *Sporochnus pedunculatus*, *Dalbergia melanozylon*, *Celastrus scandens*, *Juglans nigra*, *Kalmia latifolia*, *Pelargonium xhortorum*, *Rhus glabra* and *Lindera benzoin* (extracts); *Striga densiflora*, *Striga orobanchioides*, *Striga lutea*, *Pistacia lentiscus* L., *Mitracarpus villosus*, *Bixa orellana*, *Bridelia ferruginea*, *Alpinia katsumadai*, *Alpinia officinarum*, *Artemisia capillaris*, *Casia obtusifolia*, *Dendrobium moniliforme*, *Epimedium grandiflorum*, *Glycyrrhiza glabra*, *Lithosperum erythrorhizon*, *Magnolia obovata*, *Morus bonbycis*, *Natopterygii incisium*, *Polygonum multiflorum*, *Prunus mume*, *Rheum palmatum*, *Ricinus communis*, *Sophora flavescens*, *Swertia japonica*, black pepper, rosemary, red pepper, *Isopyrum thalictroides*, *Calotropis procera*, *Chrysanthemum* spp., *Holarrhena antidysenterica*, *Lunularia crusiata*, *Dumertiera hirsuta*, *Exormotheca tuberifera*, and liverwort (extracts); *Filipendula ulmaria*, *Salix glauca*, *Usnea filipendula*, *Clkadina arbuscula* (salicylic compounds); *Tanacetum parthenium*, *Thymus capitatus*, and *Elfingia applanata* (extracts); *Fraxinus ornus* (hydroxycoumarins, esculin, esculetin, fraxin, and fraxetin); *Zizyphus nummularia*, LONGO VITAL, *Pelargonium* spp., *Scaevola sericea*, *Psychotria hawaiiensis*, *Pipturus albidis*, *Aleurites moluccana*,

Solanum niger, *Piper methysticum*, *Barringtonia asiatica*, *Adansonia digitata*, *Harungana madagascariensis*, *Jacaranda mimosaefolia*, *Erythroxylum catauba*, *Bidens pilosa*, *Lemna minor*, *Potamogeton* spp., *Nasturtium officinale*, *Apium nodiflorum*, *Agaricus subrutilescens*, *Amanita virosa*, *Amanita pantherina*, *Lycoperdon perlatum*, *Psidium guajava*, *Averrhoa carambola*, *musa sapientum*, *Carica papaya*, *Passiflora edulis*, *Lansium domesticum* and *Baccaurea motleyana* (extracts); horse radish, celandine grass, bur marigold and yarrow grass (extracts); *Abuta grandifola*, *Cyperus articulatus*, *Gnaphalium spicatum*, *Pothomorphe peltata*, *Ficus sycomorus*, *Ficus Benjamina*, *Ficus bengalensis*, *Ficus religiosa*, *Alchornea cordifolia*, *Bridelia feruginea*, *Eucalyptus citriodora*, *Hymenocardia acida*, *Maprounea africana*, *Monachora arbuscula*, *Tedania ignis*, *Arenosclera* spp., *Amphimedon viridis*, *Polymastia janeirensis*, *Aplysina fulva*, *Pseudaxinella lunaecharta*, *Nelumbium speciosum* and *Mycale arenosa* (extracts); cloves (eugenol acetate and iso-eugenol); *Chrysthanemum boreale* (sesquiterpenoid lactones); *Eucalyptus globolus*, *Punica granatum*, *Bocconia arborea*, *Syzygium brazzavillense*, *Syzygium guineense*, *Carthamus tinctorius*), *Ginkgo biloba*, *Mosla chinensis*, *Salvia officinalis*, and *Cinnamomum cassia* (extracts); *Cryptolepis sanguinolenta* (alkaloids, cryptolepine); *Chelidonium majus* (alkaloids, berberine, coptisine); *Vitex agnus-castus* (extract); *Cladonia substellata* (usnic acid); Ellagic acid,

Fuligo septica, *Tubifera microsperma* (extract); *Mundulea monantha*, *Tephrosia linearis* (flavonoids); *Lpomoea fistulosa* (extract); *Pimenta dioica* (essential oils); *Ratibida latipalearis*, *Teloxys graveolens*, *Dodonaea viscosa*, *Hypericum calycinum*, *Hyptis albida*, *Hyptis pectinata*, *Hyptis suaveolens* and *Hyptis verticillata* (extracts); *Asteriscus graveolones* (bisabolone hydroperoxides); *Derris scandens*, *Alnus rubra*, *Araliaceae* family (extracts); *Vinca rosea*, Australian tea tree oil, peppermint oil, sage oil, thymol, eugenol and *Thuja orientalis* (extracts); *Anacardium occidentale* (phenolic lipids); *Oidiodendron tenuissimum* (extract); *Acacia nilotica* and *Acacia farnesiana* (polyphenol, tannin); *Teminalia alata* and *Mallotus phillipinensis* (extracts); *Piectranthus grandidentatus* (abientane diterpenoids); *Pumica granatum* and *Datura metel* (extracts); tea, *Agave lecheguilla*, *Chamaesyce hirta*, *Baccharis glutinosa* and *Larrea tridentata* (extracts); *Camelia sinensis* and *Euphorbia hirta* (theaflavin, polyphenon 60); *Tabernaemontana pandacaqui*, *Yucca shidigera*, *Hemistepa lyrata*, *Yougia japonica*, *Prunella vulgaris*, *Lamium amplexicaule*, *Juniperus chinensis*, *lxeris dentata*, *Gnaphalium affine*, *Chelidonium majus*, *Spirea prunifolia*, *Erythronium japonicum*, *Taxus wallichiana*, *Ganoderma lucidum Drava nemorosa*, *Youngia capillaris*, *Equisetum arvense*, Australiam Lavender, Black Seed, *Catuaba casca*, *Cineole*, *Damiana*, *Dicranum scoparium*, Eucalptus oil, Ginger, and Grape seed (extracts); Neem

seed, bark, and leaf extract; Neem oil; New Zealand Manuka extract; *Nicotiana tabacum* extract; olive leaf extract; a-pinene and b-pinene extracts; Rhubarb root extract; *Syringa vulgaris* extract; Tea tree oil (Terpinen-4-ol, a-terpinene, y-terpinene, a-terpineol, Terpinolene); Thyme (extract) and Vitamin E (extract).

Other microorganisms which may be inhibited by phytochemicals useful in the present invention are listed as follows:

Fungi
Aspergillus flavus
A. fumigalus
A. niger
Blastomyces dermatitidis
Candida spp.
Coccidioides immitis
Cryptococcus neoformans
Fusarium culmorum
Geotrichum spp.
Histoplasma capsulatum
Malassezia furfur
Microsporum spp.
Mucor racemosus
Nocardia spp.
Paracoccidioides brasiliensis
Penicillium spp.
Rhizopus higricans
Saccharomyces cerevisiae
Sporothrix schneckii
Torulopsis spp.
Trichophyton spp.
Bacteria
Aerobacter aerongenes
Aeromonas hydrophila
Bacillus cereus
Bacillus subtilis
Bordetella pertussis
Borrelia burgdorferi

Campylobacter fetus
C. jejuni
Corynebacterium diphtheriae
C. bovis
Desulfovibrio desulfurica
Escherichia coli 0157:H7
Enteropathogenic E. coli
Enterotoxin-producing E. coli
Helicobacter pylori
Klebsiella pneumoniae
Legionella pneumophila
Leptospira interrogans
Mycobacterium tuberculosis
M. bovis
Neisseria gonorrhoeae
N. meningitidis
Proteus mirabilis
P. vulgaris
Pseudomonas aeruginosa
Rhodococcus equi
Salmonella choleraesuis
S. enteridis
S. typhimurlum
S. typhosa
Shigella sonnei
S. dysenteriae
Staphylococcus aureus
S. epidermidis
Streptococcus anginosus
S. mutans
Vibrio cholerae
Yersinia pestis
Y. pseudotuberculosis
Actinomycetes
Stretomyces reubrireticuli
Streptoverticillium reticulum
Thermoactinomyces vulgaris
Viruses
Adenoviruses
Coronaviruses
Cytomegalovirus
Enteroviruses
Epstein-Barr virus

Herpes simplex virus
Hepatitis viruses
Human Immunodeficiency virus
Human Parvoviruses
Influenza viruses
Morbillivirus
Mumps virus
Norwalk viruses
Papillomaviruses
Paromyxovirus
Poxvirus
Rabies virus
Reoviruses
Rotaviruses
Rubella virus
Respiratory Synctial virus
Rhinoviruses
Varicella zoster virus

Parasites

Ancyclostoma braziliense
Anisakis
Babesia microti
Balantidum coli
Blastocystis hominis
Chilomastix mesnili
Cryptosporidium parvum
Cyclospora
Dientamoeba fragilis
Diphyllobothrium latum
Echinococcus granulosus
Entamoeba coli
E. histolytica
Enterocytozoon
Fasciola hepatica
Giardia lamblia
Iodamoeba butschlii
Isospora belli
Leishmania brasiliensis
L. donovani
L. tropica
Paragonimus westermani
Plasmodium vivax
Pnemocystis carinii

Sarcocytis hominis
Strongyloides stercoralis
Taenia solium
Toxoplasma gondii
Trichomonas vaginalis
Trichinella spiralis
Trypanosoma cruzi

The compositions of the present invention can be used in an almost limitless variety of applications. Generally, the compositions are well suited for applications where it is desirous to prevent the growth of microorganisms upon the polymeric material itself or on products in close proximity to the material. For instance, the composition can be incorporated into a container or a film for protecting the contents thereof. The following is a list of possible applications. The list is not exhaustive but is merely provided for illustrative purposes.

Floral Uses

- Plastic floral buckets
- Bucket liners
- Corsage bags
- Shredded plastic for box packing and shipping
- Starter trays
- Florafoam blocks
- Shipping and display bags for bulbs

Industrial Uses

- Containers and liners for industrial manufacturing
- Shredded plastic for packaging perishables
- Industrial pipe lining such as oil, gas and water lines
- Nuclear and hydroelectric cooling towers
- Water and sewer treatment facilities
- Aircraft fuselage interiors
- NASA applications for space
- Cat liter boxes and liners

- Swimming pool liners
- Hot tub liners

Marine Uses

- Ship and boat hulls
- Ship and boat decks and other fouling surfaces
- Buoys and mariner floating docks
- Specific Naval applications, such as optically clear underwater surfaces
- Marine rope and cable

Agricultural Uses

- Row crop plastic mulch
- Drip irrigation and related components
- Shredded Easter grass for packaging
- Seedling starter trays
- Seedling starter growing blocks
- Greenhouse related plastic components
- Granular mix for growing mediums
- Drip irrigation tubing
- Various plastic containers
- Plastic row crop tunnels
- Food packaging, wrap containers
- Retail display containers, trays, racks
- Vacuum and shrink wrap

Medical and Dental Uses

- Catheters
- Shunts
- Eye buckles
- Contact lenses
- Bandages
- Dust covers, surgical drapes
- Bed liners
- Isolation gowns, caps and shoe covers
- Clean room apparati
- Counter tops, walls and floors
- Orthopaedic appliance packaging
- Implants
- Feminine Hygiene products
- IV tubing

Miscellaneous Products

- Animal litter additive (granular)
- Animal litter container liners
- Veterinary products
- Hygiene disposal bags

Many different types of polymeric materials may be used in the present invention. A polymeric material is preferably chosen that can be formed into films, sheets, containers, tubes, granules, coatings, and laminates besides having the ability to be formed into other articles. The biocidal agents as discussed herein have been found to be compatible with a wide variety of polymers, plastics, and other materials. Preferably, the biocidal agents are placed into a hydrocarbon based material, such as by extrusion. Examples of such polymeric materials include polyalkylenes, polyolefins, polyvinyls, synthetic rubber, latex, epoxies, synthetic fiber, and mixtures thereof. Other useful polymers include polyethylenes, polypropylenes, polystyrenes, polyacrylates, polyvinylchlorides, polyurethanes, and mixtures thereof. The base material can further include homopolymers or copolymers. The particular polymer used depends mostly upon the application. For instance, polyethylene or polyvinylchloride are preferably used in plastic sheeting, liners, surgical drapes, and medical gowns because of its flexibility and physical characteristics, while latex, polyethylene glycol and polyethylene may be preferable for use in medical devices, such as shunts or catheters.

The amounts of the biocidal agents added to the composition are also dependent upon the particular application. Factors to consider are the conditions

under which the composition is to be used, the organisms to be inhibited, the duration of the use, whether the object to be protected is a consumable, and the active concentration of the antimicrobial agents that is desired. For example, capsicum can be added in an amount from about 1 ppm to about 100,000 ppm, depending upon the desired application. For a food application, capsicum could be added to the polymeric material in an amount from about .05 ppm to about 10 ppm.

It should be understood that the present invention is broadly drafted, in one embodiment, towards incorporating phytochemicals as biocidal agents into polymeric materials. In several preferred embodiments of the present invention, capsicum, citric acid extract, and grapefruit seed extract may be used as biocidal agents.

When making the compositions of the present invention, the polymeric material may or may not be heated. The biocidal agents, chemical releasers, and migration controllers are then added either together or one at a time (if more than one agent is employed in the biocide). The mixture is then mixed until the biocidal agents and the chemical releasers are evenly dispersed within the polymeric composition. Other additives, such as plasticizers and dyes, can be added without affecting the biocidal agents or the chemical releasers. In fact, some plasticizers or other ingredients may be added to enhance the resulting

physical characteristics of the composition. Accelerators such as ethylene methyl acrylate (EMA) may also be added.

The resulting composition can be extruded, blown, or molded into various articles as listed above. The following is a list of products that may incorporate the composition of the present invention.

One particular product incorporating the composition of the present invention as illustrated in Figure 1 is plastic sheeting shown generally as 10. Sheet 10 can then be formed into various packages and articles. For instance, sheet 10 can be used to make cat litter boxes. In one embodiment, a cat litter box contains capsicum in an amount of approximately 5 ppm, grapefruit seed extract in an amount of approximately 25,000 ppm and BIOCIDIN in an amount of approximately 10,000 ppm.

Referring to Figure 2, the composition of the present invention can also be incorporated into a film 20. Film 20 can be used for a variety of liners and wraps. One of the biggest problems faced by shippers and exporters of fresh produce is the relatively short life of fresh fruits and vegetables. Many produce items are shipped great distances, requiring a significant amount of travel time. Film 20 can be used to wrap fruits and vegetables for increasing their shelf life by protection from microbial infestation. Film 20 can also be used to wrap meat to increase its storage life and to inhibit microbial

organisms present after processing.

Referring to Figure 3, a liner 30 is shown made from film 20 in Figure 2. Liner 30 also may be used for a number of applications. For instance, liner 30 can be used for the transportation and shipment of cut flowers. As with produce, cut flowers typically have a short shelf life and are prone to attack by microorganisms. Liner 30 could be used to cover and protect any such plants.

Other uses for liner 30 include holding infectious wastes. With the increasing number of infectious agents, such as HIV and Hepatitis virus, transmitted via contact with blood and other bodily fluids, wastes generated by hospitals, clinics, and laboratories have created disposal concerns. Liner 30 could be used to contain such wastes and control pathogens which may leak or spill onto the outer surface of the bag and infect handlers. Liner 30 may also be used for a cat litter box liner. Preferably, the product contains capsicum in an amount of approximately 5 ppm, grapefruit seed extract in an amount of approximately 25,000 ppm and BIOCIDIN or Lemon Grass Oil in an amount of approximately 5,000 ppm. The product could be used without threat to any pets.

Figures 4 and 5 represent further articles made from the composition of the present invention. Illustrated in the figures is a floral bucket 40 and a plant starter tray 50. Biocidal agents contained

within the products protect the plants and seedlings from microbial attack. Further, the biocidal agents destroy or inhibit any harmful organisms, such as insects, larvae, or nematodes, found within the soil or in soil additives. Vitamin E may be used both as a biocidal agent and as a migration controller to retard the release of other biocides extruded in the polymeric material. Preferably, floral bucket 40 includes about 0.5 ppm capsicum, 30,000 ppm grapefruit seed extract, and approximately 15,000 ppm BIOCIDIN or Lemon Grass Oil. Plant starter tray 60 would preferably contain 0.5 ppm capsicum, 30,000 ppm grapefruit seed extract, and approximately 20,000 ppm BIOCIDIN or Lemon Grass Oil. Of course, these amounts vary depending upon the type of plant grown.

The composition of the present invention can also be extruded into particles and granules of any particular size. The particles or granules can be used in agricultural applications for nursery potting soil or for golf course greens and grass. In one particular application, the granules include grapefruit seed extract in an amount of approximately 25,000 ppm, trichloromelamine and citric acid in an amount of approximately 10,000 ppm (each), and BIOCIDIN or Lemon Grass Oil in an amount of approximately 15,000 ppm.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are Algicidals, such as Leguminose or Ericaceae, or

Antialgals, such as Liliacae or Compositae, to be incorporated into polymeric materials, with or without an antioxidant or agents, for products where the control of algae, fungi, crustaceans and/or bacteria are desired.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are antibacterials, such as Ocimum basilicum or Cuminum cyminum into a polymeric material, with or without an antioxicant agent or agents, for different types of food packaging, medical devices, or industrial products.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are anticrustacens, such as Compositae, Hyphomycetes or Artemia Salina in a polymeric material, with or without an antioxidant agent or agents, for different types of antifouling applications.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are antifungals, such as Myrtaceae, Zingiberaceae, Euphorbiaceae or Ranunculaceae incorporated with a polymeric material, with or without an antioxidant agent or agents, for different types of devices where fungal protection is desired, such as military aircraft, athlete and leisure wear, and containers.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are antinematodals, such as Compositae, Leguminosae or

Umbelliferae, incorporated into polymeric materials, with or without and antioxidant agent or agents, for different types of products where the control of nematodes is desired. Examples include: potting soil granules, hydro-soluble substrates for soil treatment, or plastic planting pots and other related agricultural products where nematode control is desired.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are antivirals, such as Punicaceae, Rosaceae, Labiatae and Umbelliferae incorporated with polymeric materials, with or without an antioxidant agent or agents, for different devices where viral control is desired. Examples include plastic food wrap, medical gowns and devices.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are antiyeasts, such as Libiatae, Myrtaceae, or Umbelliferae incorporated in a polymeric material, with or without an antioxidant agent or agents, for devices where the control of yeast infection is a factor. Examples include vaginal apparati or food packaging.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are insecticides, such as Annonaceae, Ericaceae, or Piperaceae in a polymeric material, with or without an antioxidant agent or agents, for devices where insect

control is desired. Examples include pet collars and bedding, spray applications or food packaging.

As an example, this invention claims the use of phytochemicals, alone or in combination, that are Molluscidals, such as Cyperaceae, Leguminosae, or Myrtaceae, in a polymeric material, with or without an antioxidant agent or agents, for applications where mollusk growth is a problem, such as marine or industrial surfaces.

This invention expands on the names and claims of antioxidants, beyond Vitamin E. A comprehensive list of phytochemicals with antioxidant characteristics have also been listed in the Specification above. In addition to the list in the Specification, the following antioxidants are also claimed: Vitamin E, Lysine, BHT (Butykatehydroxytoluene), BHA (Butylatedhydroxyanisole), Grape seed extract and Pine Bark extract(Proanthocyanidins), Beta Carotene, Bilberry extract, Ascorbic Acid, Ginkgo Biloba Extract, Green Tea Extract, Turmeric, Zinc Picolinate, and Selenium. These antioxidants, along with the list of phytochemical antioxidants listed tn the exhibit may by used alone or in combination with phytochemicals. For example, there is a synergistic effect combining vitamin E and yeast-free Selenium.

The composition of the present invention also may be molded or extruded into a variety of medical devices, including tubing, shunts, implants and catheters.

The present invention may be better understood by reference to the following example.

EXAMPLE

The following study was conducted to determine bacterial counts obtained from chicken stored in biocidal films, as compared to that wrapped in commercial plastic packaging film.

Chicken parts were packaged in film at a commercial facility and kept at temperatures below 38°F. prior to testing. Two types of biocidial films were tested. Mag 1 was made by extruding capsicum into PVC 60 gauge film at 1.7 ppm plus Vitamin E at 2,000 ppm. Mag 2 was made by extruding zinc pyrithione at a concentration of about 1,000 ppm plus Vitamin E at a concentration of about 2,000 ppm. Control film consisted of commercial plastic wrap. From each package, triplicate samples were collected at varying intervals (days 0, 3, 6, 9, 12, 14 and 18), plated onto appropriate media, and bacterial counts determined. Counts for days 0, 3, 9, and 12 were obtained by plating samples from a 100 ml rinse obtained from the chicken. Day 18 counts were determined from 25 g pieces of chicken, excised and diluted 1:10 with BPB before culture, while day 14 counts were determined for both rinse and excision samples.

The study showed that there were no significant differences in bacterial counts between experimental samples wrapped in antimicrobial wrap and controls

wrapped in commercial film, when cultures were obtained from rinse samples. These results indicate that the biocidal film must be in close contact with the material, in order to inhibit microorganisms. Therefore, Day 14 samples were cultured from a 25g excision piece of chicken, as well as from the 100 ml rinse. The samples cultured at Day 18 were obtained solely from the excision method.

Table 1 shows Day 14 and Day 18 bacterial counts, obtained from 25g chicken samples wrapped in control film, as compared to samples from chicken wrapped in two concentrations of biocidal film, Mag 1 and Mag 2.

TABLE 1 - BACTERIAL COUNTS FROM 25g EXCISION SAMPLES

	TPC35°C	TPC20°C	TPC5°C	LAC30°C	LAC20°C	LAC5°C	E.coli	Coliform
Control Day 14	9.31E+05	3.40E+06	4.43E+06	1.44E+04	1.13E+04	1.00E+01	1.00E+01	4.67E+01
Mag 1 Day 14	3.72E+05	3.35E+06	2.18E+06	2.60E+03	2.20E+03	1.00E+01	1.00E+01	1.00E+01
Mag 2 Day 14	5.37E+04	5.53E+05	1.01E+06	2.93E+03	2.84E+03	1.00E+01	1.00E+01	1.00E+01
Control Day 18	3.64E+07	6.67E+07	4.59E+07	3.38E+05	4.00E+05	1.00E+01	1.00E+02	2.00E+02
Mag 1 Day 18	5.80E+05	3.87E+06	2.78E+07	3.13E+03	3.33E+03	1.00E+01	1.00E+02	1.00E+02
Mag 2 Day 18	2.98E+07	3.61E+07	4.93E+06	1.09E+05	1.42E+03	1.00E+01	1.00E+02	1.03E+03

Mag 1 = 1.7 ppm capscium plus 2,000 ppm Vitamin E; Mag 2 = 2500 ppm pyrithione plus 2000 ppm Vitamin E; Control = Commercial Plastic Wrap; TPC = total plate count;
LAC = Lactic acid bacteria count; E.coli = E.coli colonies; Coliform = Coliform colonies

Results: Both Day 14 and Day 18 total plate counts (TPC) show a significant decrease in samples from Mag 1 or Mag 2 film, as compared to controls, at the majority of the time points tested. Only the Day 14 Mag 1 sample, incubated at 20°C., showed no significant TPC reduction as compared to the control count.

Similar results were seen when comparing lactic

acid bacteria counts (LAC) between experimental samples (Mag 1 or Mag 2 film) and controls. A significant reduction in bacteria numbers was seen in all experimental groups, as compared to controls, except samples incubated at 5°C.

The incubation of samples for *E. coli* counts did not show any differences between the number of colonies isolated from control plates, as compared to experimental samples. However, the total number of *E. coli* colonies cultured was too low to permit the drawing of any meaningful conclusions.

At both Day 14 and Day 18, the number of coliform bacteria cultured from chicken samples wrapped in Mag 1 or Mag 2 showed a significant reduction as compared to controls, at all time points with one exception. The Day 18 sample from chicken wrapped in the Mag 2 film did not show a reduction in coliform colonies.

The results of this study show that wrapping chicken in a biocidal film, such as Mag 1 (containing 1.7 ppm capsicum plus 2,000 ppm Vitamin E in a 60 gauge PVC polymer) or Mag 2 (containing zinc pyrithione plus 2,000 ppm Vitamin E in a 60 gauge PVC polymer), can significantly inhibit associated bacteria.

It should be understood that the present invention is not limited to the specific compositions or methods described herein and that any composition having a formula or method steps equivalent to those described falls within the scope of the present

invention. Preparation routes of the composition and method steps for controlling the release of antimicrobial agents are merely exemplary so as to enable one of ordinary skill in the art to make the composition and use it according to the described process and its equivalents. It will also be understood that although the form of the invention shown and described herein constitutes preferred embodiments of the invention, it is not intended to illustrate all possible forms of the invention. The words used are words of description rather than of limitation. Various changes and variations may be made to the present invention without departing from the spirit and scope of the following claims.

WHAT IS CLAIMED IS:

1. A polymeric material containing antimicrobial agents for inhibiting the growth of microorganisms in close proximity to said polymeric material, said polymeric material comprising:

a polymeric substrate; and

at least one biocide dispersed within said polymeric substrate, said biocide being present in said polymeric substrate in an amount sufficient to inhibit the growth of microorganisms that come in contact with said polymeric substrate, said at least one biocide comprising a phytochemical derived from a naturally occurring source.

2. A polymeric material as defined in claim 1, wherein said phytochemical is a material selected from the group consisting of capsicum, grapefruit seed extract, lemon grass oil, tea tree oil, citric acid, and mixtures thereof.

3. A polymeric material as defined in claim 1, further comprising a release agent for facilitating release of said at least one biocide from said polymeric substrate, said release agent comprising citric acid.

4. A polymeric material as defined in claim 1, further comprising Vitamin E dispersed within said polymeric substrate.

5. A polymeric material as defined in claim 1, wherein said at least one biocide is contained in a liquid carrier when dispersed within said polymeric

substrate.

6. A polymeric material as defined in claim 5, wherein said liquid carrier comprises an epoxidized vegetable oil or propylene glycol.

7. A polymeric material as defined in claim 1, wherein said at least one biocide is present in said polymeric substrate in an amount up to about 100,000 ppm.

8. A polymeric material as defined in claim 1, wherein said at least one biocide is present within said polymeric substrate in an amount up to about 50,000 ppm.

9. A polymeric material as defined in claim 1, wherein said at least one biocide comprises a mixture of chlorophyll, impatiens, pallida, hydrastis canadensis, ferula galbanum, hypericum perforatum, villa rubris, fumaria, frasera carolinesis, gentiana campestris, sanguinaria, allicin and garlic.

10. A polymeric material containing antimicrobial agents for inhibiting the growth of microorganisms in close proximity to said polymeric material, said polymeric material comprising:

a polymeric article, said polymeric article being made from a polymer selected from the group consisting of silicones, polystyrenes, polyacrylates, polyurethanes, polyalkylenes, polyolefins, polyvinyls, synthetic rubbers, epoxies, latex, N-propylsilicate and mixtures thereof;

a release agent; and

at least one biocide dispersed within said polymeric article, said biocide being present in said polymeric article in an amount sufficient to inhibit the growth of microorganisms that come in contact with said polymeric article, said release agent being present to control release of at least one biocide from said polymeric article, said biocide comprising a phytochemical derived from a naturally occurring source, wherein said phytochemical is selected from the group consisting of capsicum, grapefruit seed extract, lemon grass oil, tea tree oil, citric acid, and mixtures thereof.

11. A polymeric material as defined in claim 10, wherein said release agent comprises citric acid.

12. A polymeric material as defined in claim 10, wherein said release agent comprises Vitamin E.

13. A polymeric material as defined in claim 10, wherein said biocide is contained in a liquid carrier.

14. A polymeric material as defined in claim 10, wherein said polymeric article comprises a plastic film.

15. A polymeric material as defined in claim 10, wherein said polymeric article comprises a plastic container.

16. A polymeric material as defined in claim 10, wherein said phytochemical is capsicum.

17. A polymeric material as defined in claim 10, wherein said phytochemical is grapefruit seed extract.

18. A polymeric material as defined in claim 10,

wherein said phytochemical is tea tree oil.

20. A polymeric material as defined in claim 17, wherein said polymeric article is a catheter comprising latex.

21. A polymeric article as defined in claim 20, wherein said phytochemical is grapefruit seed extract.

22. A polymeric article as defined in claim 20, wherein said phytochemical is tea tree oil.

23. A polymeric article as defined in claim 10 wherein said release agent comprises said biocide.

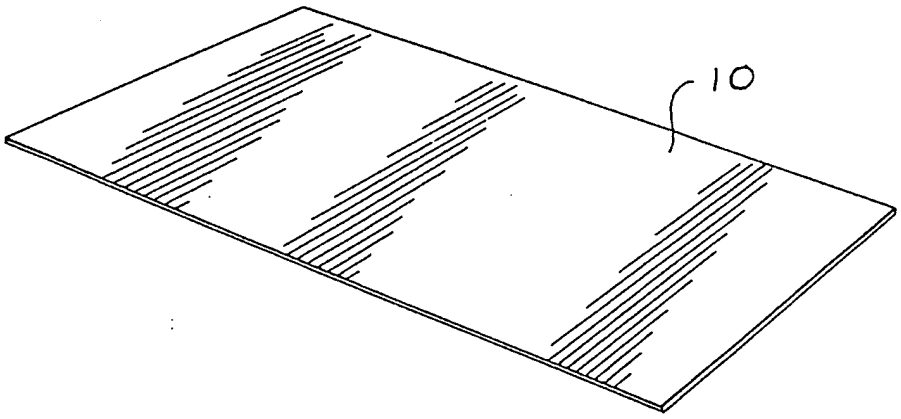

Fig. 1

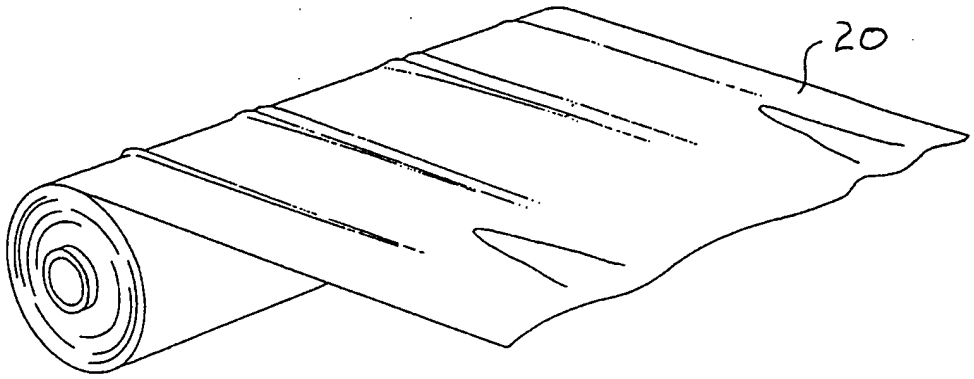

Fig. 2

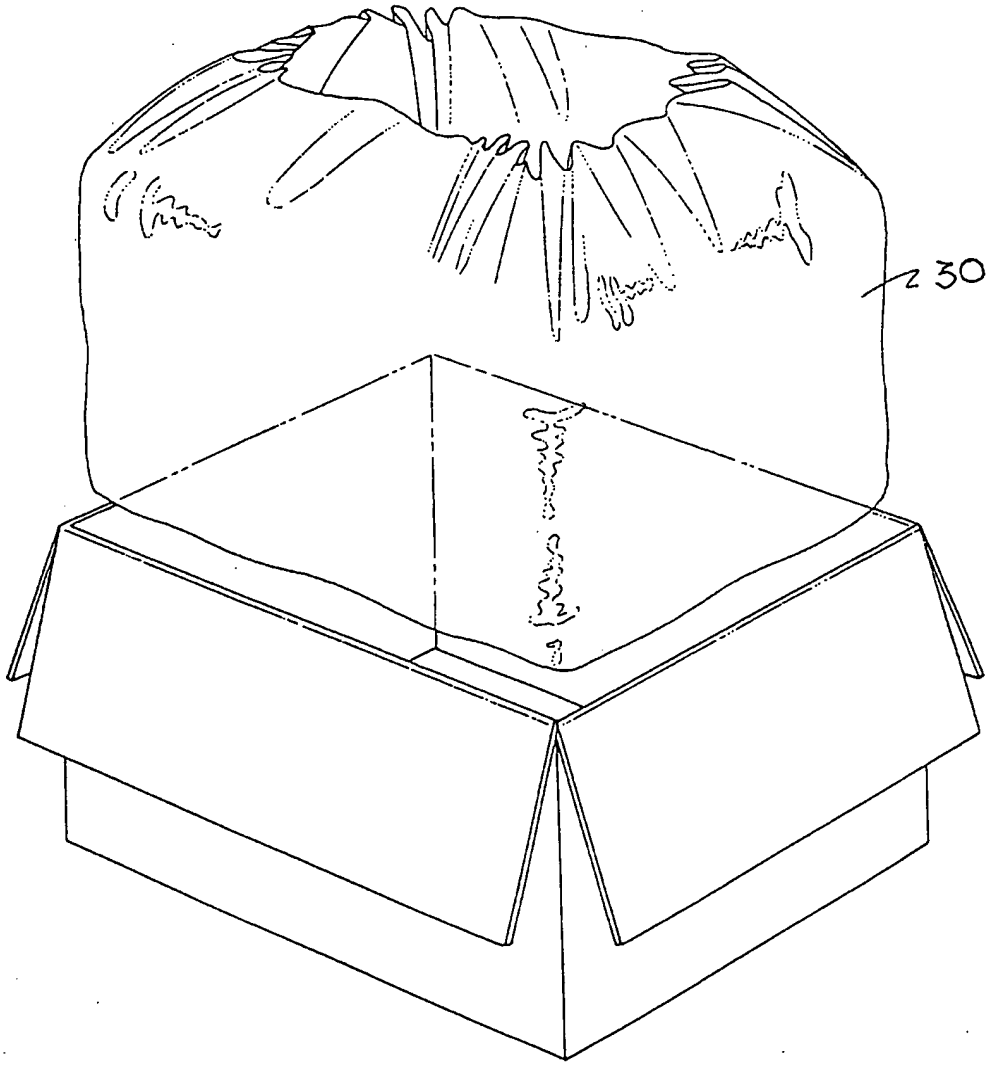

Fig. 3

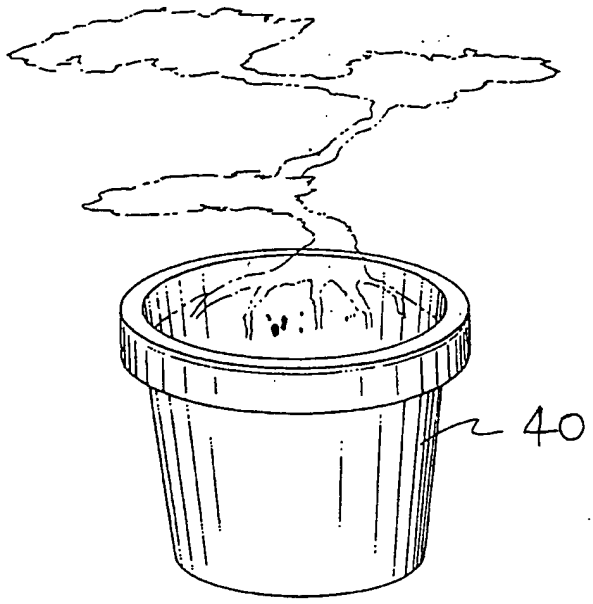

Fig. 4

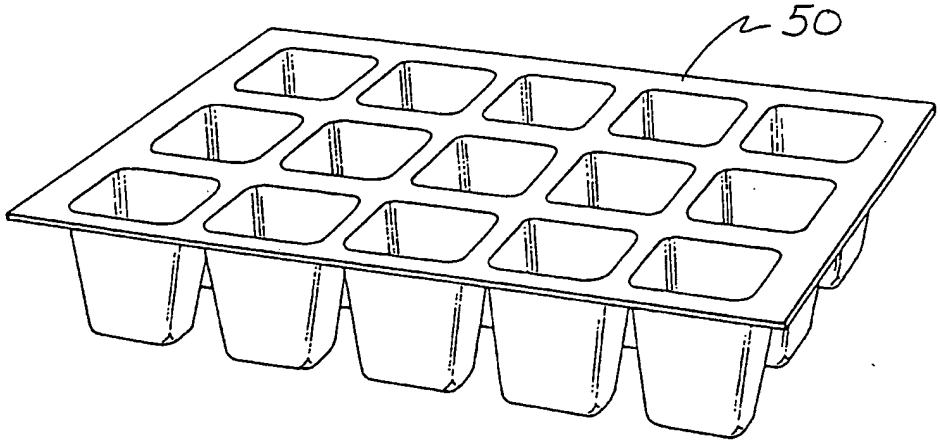

Fig. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/22157

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 9/70

US CL : 424/405, 408, 402, 404

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/405, 408, 402, 404

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2,566,410 A (GRIFFIN et al) 04 September 195/., see entire document.	1-23
A	US 4,978,686 A (SOTOME) 18 December 1990, see entire document.	1-23
A	US 5,079,000 A (TAKAHASHI et al) 07 January 1992, see entire document.	1-23
A	US 5,554,373 A (SEABROOK et al) 10 September 1996, see entire document.	1-23
A	US 5,466,459 A (WILSON) 14 November 1995, see entire document.	1-23
A	US 5,639,794 A (EMERSON et al) 17 June 1997, see entire document.	1-23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
31 JANUARY 1999	22 FEB 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer THURMAN K. PAGE Telephone No. 703-308-1234

Form PCT/ISA/210 (second sheet)(July 1992)*